New York State Agricultural Experiment Station
CORNELL UNIVERSITY GENEVA • NEW YORK

DEVELOPMENT OF THE "GENE GUN" AT CORNELL

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GENEVA, NY: The development of the gene gun in the early 1980's revolutionized the science of genetic engineering and ushered in the age of genetic transformation in the United States and the world. This pioneering advance was developed by Cornell University plant scientists at the New York State Agricultural Experiment Station at Geneva, N.Y., and researchers and engineers at the Cornell Nanofabrication Facility (CNF).

Horticultural scientists John Sanford and Theodore Klein at the Geneva Station sought the assistance of the Nanofabrication Facility in developing a device that could streamline traditional plant breeding practices by injecting genes directly into plant nuclei and tissues. What was needed was a means by which genetic material carrying desirable characteristics, such as drought or pest resistance in plants, could be coated onto microparticles and then accurately "shot" into living cells and tissues, thereby altering their genetic makeup. What was eventually fashioned and refined by Sanford with the help of CNF experts Edward Wolf and Nelson Allen was the Biolistic Particle Delivery System–or so-called "gene gun."

Applications of its use are many and diverse. For example, biologists at Cornell and Washington universities have genetically engineered and successfully field tested rice plants that resist some of the most destructive insects as well as salt and drought damage. Technology for the transgenic rice plants, which incorporates genes from potato plants to resist insect damage and genes from barley plants to make them salt- and drought-tolerant, will be given to developing countries under provisions of a Rockefeller Foundation grant. Rights to the technology, which potentially can reduce crop losses by billions of dollars each year, will be sold in developed countries such as the United States and Japan.

In another application that represents the first instance of commercializing a genetically-engineered, virus-resistant, perennial fruit crop, the gene gun was used to create virus-resistant seed that is expected to save Hawaii's $45 million-a-year papaya industry from the onslaught of a killer virus.

In a third example closer to home, Cornell University researchers have identified one of the biological weapons used by a fungus that preys on other fungi, paving the way for environmentally friendly ways to control problems ranging from plant rot to bathroom mold. The gene gun was used to test expression of the fungi's suppressive effects in wine grapes important in New York State, which should lead to agricultural applications that advantage New York grape growers in their perennial fight against fungus damage.

HOW THE GENE GUN WORKS

The gene gun is one of several methods used by genetic engineers in the application of recombinant DNA technology. Central to the technology is the ability to isolate genes, direct their expression of protein, monitor inheritance, reintroduce the DNA into plant cells, develop plants from those cells, grow plants that are viable in the lab, in the greenhouse, in field trials, and finally in commercial acreage.

To better understand the technology, it is useful to remember that the characteristics of all living organisms are

determined by the information contained within DNA that is inherited from their parents. Mapping of genes and advances in the coding sequences for plant expression in the past 20 years allow scientists to manipulate DNA in much the same that engineers manipulate videotape. DNA and videotape are linear information systems that carry encoded information. That information can be decoded, expressed, copied, spliced, and edited. More copies–i.e., more plants–can be made from the edits. The new "tape" is intellectual property; so gene sequences–like videos–can be licensed, patented, and sold. Where there is money to be made, there is commercially viable technology and license agreements to be negotiated. After the lawyers are satisfied, commercialization begins and the technology begins to reach the growers and the consumers for whom it was originally intended.

The gene gun is a biolistic process that transfers isolated DNA into the chromosomes of plant cells. At the Geneva campus, "Father Gun" and "Son of a Gun" reside on the second floor of Hedrick Hall. These gene gun prototypes were developed by Sanford who eventually sold the technology to duPont under licensing agreement with the Cornell Research Foundation (CRF).

The "gun" consists of two small 6" x 7" x10" stainless steel chambers connected to a 2HP vacuum pump. When the technician flicks the switch on the outside of the second chamber, helium is released at 1000 psi. The blast ruptures a disk about the size of a nickel. The explosion of the disk releases a shock wave which travels 1 centimeter until it hits another disk, which is free to move. Attached to the front of that disk are microscopic tungsten particles 1 micron in diameter coated with thousands of DNA molecules. This disk travels another centimeter at the speed of a rifle bullet, roughly 1300 feet per second, and hits a screen, which detains the disk, but "launches" the microscopic particles toward the target cells. The particles penetrate the cells and release the DNA, which is diffused into the nucleus and incorporated by the chromosomes of the plant. In work with papaya, for example, the plant cells were thereby "coded" for PRSV resistance by this gene transfer. When all went as designed, they became the parent plants of disease resistant papaya.

In all genetic engineering trials, researchers have to be sure the technology has worked. Sometimes it fails; other times it damages the target cells. Following the expression of the DNA into the papaya cells by the gene gun, for instance, researchers tested what they hoped were the genetically altered cells to make sure the desired gene transfer had occurred by subjecting the cells to the antibiotic Kanamycin. Only disease resistant cells survive Kanamycin. The cells were then carefully regenerated in petri dishes in sterile, growth chambers.

Tissue culture is one of the most difficult aspects of genetic engineering and a very delicate task. At every stage of development, scientists test the tissue for viability and disease resistance by subjecting it to the target disease. At first, they do this in petri dishes, later in the greenhouse, then in field trials, and, finally, on commercial acreage.

FUNDING FOR THE GUN

Noteworthy in the story of the gene gun's development is that there was never direct grant support from the National Science Foundation (NSF) to the Cornell scientists for its development. Rather, it was the Foundation's establishment of the Nanofabrication Facility as a national research center at Cornell that afforded the opportunity for cross-disciplinary collaboration and access to the engineering/fabrication expertise that ultimately led to development of a viable gene gun device. Such "cross-fertilization" of ideas and collaborative applications are goals of NSF's national research centers approach. (Cornell is currently home to five national research centers, all receiving base support from the National Science Foundation [NSF]. These include the Center for High Energy Synchrotron Studies, the Floyd R. Newman Laboratory of Nuclear Studies, the National Astronomy and Ionosphere Center [which operates the world's largest radio-radar telescope in Arecibo, Puerto Rico], the Cornell Nanofabrication Facility [CNF], and the National Science and Technology Center for Computer Graphics and Scientific Visualization.)

Technology rights to the gene gun technology were sold to the duPont Company in 1990, resulting at that time in the largest payment ever made to Cornell for royalties under a patent.

Dr. Sanford continued to develop and collaborate on gene gun applications specific to horticulture at Cornell until 1998.

Clearly, the gene gun and its use has revolutionized genetic engineering in many fields. In a reflection of its importance in the new age of genetics, a prototype of the gene gun is on display at the Smithsonian Institution's Museum of American History in Washington, D.C. as part of its "New Frontiers" exhibit, as well as at EPCOT Center in Orlando, FL.

There is an article on Dr. Sanford here.

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